SUNFISH Parts 1 and 2: 4-year efficacy and safety of risdiplam in Types 2 and 3 spinal muscular atrophy (SMA)


SUNFISH (NCT02908685) is a two-part clinical trial of risdiplam in a broad and heterogeneous patient population with Types 2 and 3 SMA in four countries.

Part 1 was a dose-finding study, which determined the dose for Part 2.

- Part 2 is the confirmatory study assessing the efficacy of risdiplam at dose determined in Part 1.

The primary outcome is the change from baseline in MFM32 total score at Month 48.

Part 2 was a placebo-controlled, double-blind study with broad inclusion criteria and a large dataset.

A randomized, placebo-controlled, double-blind study with broad inclusion criteria and a large dataset.

Background

- SMA is a severe progressive neuromuscular disease leading to loss of muscle function and a reduced life expectancy.
- Risdiplam is a centrally and peripherally distributed oral drug that increases SMN2 copy number.

Patient baseline characteristics

<table>
<thead>
<tr>
<th>Part 1</th>
<th>Part 2</th>
<th>Total (N=160)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at screening, years (median (IQR))</td>
<td>7.0 (3.4–12.5)</td>
<td>6.4 (3.5–12.2)</td>
</tr>
<tr>
<td>Age at diagnosis, years (median (IQR))</td>
<td>3.4 (1.3–6.1)</td>
<td>3.4 (1.2–6.0)</td>
</tr>
<tr>
<td>Gender, female, n(%)</td>
<td>18 (32.1)</td>
<td>18 (32.1)</td>
</tr>
<tr>
<td>SMA type, n (%)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>36 (65.3)</td>
<td>36 (65.3)</td>
</tr>
<tr>
<td>n (%)</td>
<td>111 (19.3)</td>
<td>111 (19.3)</td>
</tr>
</tbody>
</table>

Mean change from baseline in SMAIS-ULM total score*†:

- In Part 1: n=58
- In Part 2: n=59
- Overall: n=117

- The increase in RULM total score from baseline over 24 months was sustained up to Month 48 with risdiplam treatment.

- Without treatment patients with Types 2 and 3 SMA show a decline in baseline motor function scores.

- Risdiplam (n)|| 115 113 113 112 107 103 85 100 101 98 Patients (n)|| 112 103 100 98 112 103 100 98
- Placebo (n)† 58 57 56 56

**Results are shown for the placebo arm received placebo for 12 months followed by risdiplam treatment. Risdiplam period not shown in this graph.**

Additional exploratory efficacy motor function analyses over 48 months

- Change from baseline in SMAIS-ULM total score:

- The increase in RULM total score from baseline over 24 months was sustained up to Month 48 with risdiplam treatment.

- Without treatment patients with Types 2 and 3 SMA show a decline in baseline motor function scores.

- Risdiplam is a centrally and peripherally distributed oral drug that increases SMN2 copy number.

- SMA is a severe, progressive neuromuscular disease leading to loss of muscle function and a reduced life expectancy.

- Survival of motor neuron (SMN) is an essential gene for the maintenance of spinal motor neurons.

- SMA is caused by a decrease in the number of functional SMN protein.

- Risdiplam has been approved for the treatment of patients with SMA in over 150 countries and states.

- SUNFISH (NCT02908685) is a two-part clinical trial of risdiplam in a broad and heterogeneous patient population with Types 2 and 3 SMA.

- Part 1 was a dose-finding study, which determined the dose for Part 2.

- Part 2 is the confirmatory study assessing the efficacy of risdiplam at the dose determined in Part 1.

- The primary outcome is the change from baseline in MFM32 total score at Month 48.

- Treatment adherence was high in SUNFISH Parts 1 and 2 (91.0%–98.2%).

- There have been no treatment-related AEs leading to withdrawal or treatment discontinuation.

**Please scan using your QR reader application to access the graphs and data presented in this presentation and additional information. NB: there may be associated costs for downloading data. These costs will be in US$. Please check with your local data supplier or contact your service provider for more details. Alternating text can be accessed at https://www.roche.com/media/releases/med-cor-2022-10-12.

SUNFISH Parts 1 and 2: overall rate of AEs and SAEs per 100PY

- There have been no treatment-related AEs leading to withdrawal or treatment discontinuation.

- Patients and caregivers reported stabilization or continuous improvements in the SMAIS-ULM total score change from baseline with risdiplam treatment over 48 months.

- Increases in motor function scores were sustained after 4 years.

- Patients and caregivers reported stabilization or continuous improvements in the SMAIS-ULM total score change from baseline with risdiplam treatment over 48 months.

- These results confirm the longer-term efficacy and safety of risdiplam in a broad and heterogeneous population of individuals with Type 2 and non-ambulant Type 3 SMA.

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SUNFISH Parts 1 and 2: the observed AP profile over 48 months was reflective of underlying disease

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*Supplementary information – the content below was not in the poster presented at MDA 2023 but is available via a QR code.

A total of 8% (14/180) of patients discontinued from SUNFISH Part 2 over 48 months.

In SUNFISH Part 1, increases in MFM32 total score from baseline were maintained between Months 12 and 48 in patients treated with risdiplam.

Abbreviations
- CI, confidence interval
- COVID-19, coronavirus 2019
- MFM32, 32-item Motor Function Measure

Supplementary material

Table showing patients' status and reasons for discontinuation over time.

Graph illustrating the mean change from baseline in MFM32 total score over time.

Supplementary material – please scan QR code.